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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/782,588	KAIN ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-12 and 18-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-12 and 18-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1-4, 6-12 and 18-25, filed 28 March 2002 in Paper No. 8 is acknowledged.

Applicant's amendments of Claims 6 and 8 in Paper No. 8 are acknowledged.

Applicant's cancellation of Claims 5, 13-17 and 26 in Paper No. 8 is acknowledged.

Claims 1-4, 6-12 and 18-25 are pending and discussed below.

Information Disclosure Statement

2. The references listed on the 1449 received 11 June 2001 in Paper NO. 5 and 15 October 2001 in Paper No. 6 have been reviewed and considered. Additionally, the International Search Report filed with Paper No. 6 has been considered.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, Provisional Application 60/181,631 filed 2 February 2000 upon which priority is claimed does not provide adequate support under 35 U.S.C. 112 for claims 1-4, 6-12 and 18-25 of this application. Specifically, the '631 application does not teach or describe a first and second subpopulation of microspheres; does not teach or describe random distribution of microspheres on a substrate surface; does not teach or describe a distance between centers of a first and second microsphere subpopulations; and does not teach or describe a ratio of first and second subpopulations. Because the '631 application does not teach or describe the above limitations recited in the instant claims, the '631 application does not provide adequate support under 35 U.S.C. 112, for the instant claims. Therefore, the effective filing date for the instant claims is the filing date of the instant application i.e. 12 February 2001.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-4 and 6-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4 and 6-12 are indefinite for the recitation "is formatted to the dimensions of a microscope slide" because it is unclear whether the recitation is a method step of formatting the substrate. Therefore, it is unclear what structural limitations the method step imposes on the claimed microscope slide composition. It is suggested that Claim 1 be amended to describe the structural limitations of the microscope slide composition e.g. replace "is formatted to" with "comprises" (page 9, lines 24-29).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-4, 6-12, 18-20 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Demers et al (U.S. Patent No. 5,840,256, issued 24 November 1998) in view of Van Ness et al (U.S. Patent No. 6,248,521, issued 19 June 2001) and Walt et al (WO 98/40726, published 17 September 1998).

Regarding Claim 1, Demers et al teach a composition comprising: a substrate with a surface comprising discrete sites said site separated by a distance of less than 50m m (Column 4, lines 14-23 and Fig. 1); and a population of microspheres (Column 5, lines 30-31) comprising at least a fist and a second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent (Column 6, lines 10-26). Additionally, Demers et al teaches the dimensions of the substrate is determined based on compatibility with illuminating means (Column 5, lines 55-56) but they do not specifically teach the substrate is formatted to the dimensions of a microscope slide. However, it was well known in the art a the time the claimed invention was made that microspheres on substrate having the dimensions of a glass slide are easily illuminated and detected using a microscope as taught by Van Ness et al (Column 19, lines 27-41). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Demers et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 19, lines 27-30) and as suggested by Demers et al (Column 5, lines 55-56). Demers et al teach the substrate comprises microspheres (Column 5, lines 30-31) but they are silent regarding random or non-random distribution of said microspheres. However, randomly distributed microspheres were well known in the art at the time the claimed invention was made as taught by Walt et al. Specifically, Walt et al teach a similar composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μ (Fig. 5); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (page 17, line 13-page 18, line 24) wherein the randomly distributed microspheres are detectable based on signal and eliminates

the need to address agent-specific microspheres on the substrate (Abstract). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the randomly distributed microspheres of Walt et al to the microsphere distribution of Demers et al thereby eliminating microsphere addressing for the obvious benefits of eliminating an unnecessary step. The courts have stated that it would be obvious to omit an element when a function attributed to said element is not desired or required (see Ex parte Wu, 10 USPQ 2031).

Regarding Claim 2, Demers et al teach the composition wherein said sites are separated by a distance of less than 25m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 3, Demers et al teach the composition wherein said sites are separated by a distance of less than 15m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 4, Demers et al teach the composition wherein said sites are separated by a distance of less than 15m m (Column 4, lines 14-23 and Fig. 1) but they do not teach the separation is at least 5m m. However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation distance of Demers using routine experimentation to thereby derive an optimal separation distance (e.g. at least 5m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claims 6 and 7, Demers et al teach the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 2.2m m (Column 4, lines 20-21) which is less than 100m m as claimed in Claim 7. And they teach the pitch is determined/selected based on a number of factors e.g. substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with

illumination means (Column 4, line 59-Column 5, line 15) but they do not specifically teach the distance between centers is at least 5m m (Claim 6) and less than about 100m m (Claim 7). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Demers using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5m m and less than 100m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 8, Demers et al teach the composition wherein said substrate further comprises first and second assay locations (i.e. cell) wherein said first and second subpopulations are distributed in said assay locations (Claim 1).

Regarding Claim 9, Demers et al teach the composition wherein the distance between the first and second microsphere is less than 100m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 10, Demers et al teach the composition wherein the distance between the first and second microsphere is less than 50m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 11, Demers et al teach the composition wherein the distance between the first and second microsphere is less than 15m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 12, Demers et al teach the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 2.2m m (Column 4, lines 20-21) and they teach the pitch is determined/selected based on a number of factors e.g. substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means (Column 4, line 59-Column 5, line 15) but they do not specifically teach the distance between centers is at least 5m m. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was

made to modify the distance between centers of the first and second subpopulations on the substrate of Demers using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

Regarding Claim 18, Demers et al teach a method for making a microscope slide composition comprising: providing a substrate with a surface comprising discrete sites said site separated by a distance of less than 50m m (Column 4, lines 14-23 and Fig. 1); and distributing a population of microspheres (Column 5, lines 30-31) comprising at least a fist and a second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent (Column 6, lines 10-26). Additionally, Demers et al teaches the dimensions of the substrate is determined based on compatibility with illuminating means (Column 5, lines 55-56) but they do not specifically teach the substrate is formatted to the dimensions of a microscope slide. However, it was well known in the art a the time the claimed invention was made that microspheres on substrate having the dimensions of a glass slide are easily illuminated and detected using a microscope as taught by Van Ness et al (Column 19, lines 27-41). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Demers et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 19, lines 27-30) and as suggested by Demers et al (Column 5, lines 55-56). Demers et al teach the substrate comprises microspheres (Column 5, lines 30-31) but they are silent regarding random distribution of said microspheres. However, randomly distributed microspheres were well known in the art at the time the claimed invention was made as taught by Walt et al. Specifically, Walt et al teach a similar method comprising providing a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μ (Fig. 5); and

randomly distributing a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (page 17, line 13-page 18, line 24) wherein the randomly distributed microspheres are detectable based on signal and eliminates the need to address agent-specific microspheres on the substrate (Abstract). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the randomly distributed microspheres of Walt et al to the microsphere distribution of Demers et al thereby eliminating microsphere addressing for the obvious benefits of eliminating an unnecessary step. The courts have stated that it would be obvious to omit an element when a function attributed to said element is not desired or required (see Ex parte Wu, 10 USPQ 2031).

Regarding Claim 19, Demers et al teach the method wherein said wells are separated by a distance of less than 25m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 20, Demers et al teach the method wherein the wells are separated by a distance of less than 15m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claims 23 and 24, Demers et al teach the method wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 2.2m m (Column 4, lines 20-21) and they teach the pitch is determined/selected based on a number of factors e.g. substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means (Column 4, line 59-Column 5, line 15) but they do not specifically teach the distance between centers is at least 5m m (Claim 23) and at least 15 m m (Claim 24). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Demers using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5m m and at least 15m m) for

the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 25, Demers et al teach the method wherein the distance between microspheres is at least 2.2m m (Column 4, lines 20-21) and they teach the spacing is determined/selected based on a number of factors e.g. substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means (Column 4, line 59-Column 5, line 15) but they do not specifically teach the distance between microspheres is at least 50m m. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between microspheres on the substrate of Demers using routine experimentation to thereby derive an optimal distance (e.g. at least 50m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

8. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Demers et al (U.S. Patent No. 5,840,256, issued 24 November 1998) in view of Van Ness et al (U.S. Patent No. 6,248,521, issued 19 June 2001), Walt et al (WO 98/40726, published 17 September 1998) and Gentalen et al (U.S. Patent No. 6,306,643 B1, filed 24 August 1998).

Regarding Claims 21 and 22, Demers et al is silent regarding a ratio between microsphere subpopulations. However, ratios of subpopulations were well known in the art at the time the claimed invention was made as taught by Gentalen et al who teach that subpopulation ratios are derived based on experimental design (Column 11, lines 13-44 and

Claim 9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the ratio of first and second subpopulations based on experimental design to thereby optimize experimental results. For example, for an experiment designed to detect nucleic acid sequences expressed in low copy number, the skilled practitioner in the art would have been motivated to provide subpopulations of nucleic acid microspheres in a ratio of 1:36 or 1:100 (high copy number sequence:low copy number sequence) to thereby detect the low copy number sequence without signal interference from the high copy number sequence. In this experimental design it would have been obvious to one of ordinary skill in the art to modify the low copy to high copy number ratio using routine experimentation to thereby optimize experimental conditions to maximize detection of low copy number sequences.

9. Claims 1-4, 6-12, 18-20 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 998/40726, published 17 September 1998) in view of Noonan et al (U.S. Patent No. 6,129,896, filed 17 December 1998) and Van Ness et al (U.S. Patent No. 6,248,521, issued 19 June 2001).

Regarding Claim 1, Walt et al teach a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μ (Fig. 5); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (page 17, line 13-page 18, line 24). Walt et al teach that the substrate comprises a plurality of fibers arranged into a bundle for optimal observation via their microscope objective lens (page 19, lines 15-25) but they do not teach their substrate is formatted to the dimensions of a microscope slide. However, it was well known in the art at the time the claimed invention

was made that fiber optic bundles can be formatted to desired dimensions as taught by Noonan et al. (Abstract) and Van Ness et al teach a motivation for formatting the substrate to have the dimensions of a microscope slide i.e. a substrate having the dimensions of a glass slide is easily illuminated and detected using a microscope (Column 19, lines 27-41). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Walt et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 19, lines 27-30).

The courts have stated that claimed dimensions of a known device do not distinguish over the prior art device when the claimed device would not perform differently from the prior art device. *In Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

The courts have stated that absent evidence to the contrary, a particular configuration of a known device is a matter of choice which would have been obvious to one skilled in the art. *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966) (The court held that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.).

Regarding Claim 2, Walt et al teach the composition wherein the sites are separated by a distance of less than 25 m m (Fig. 5).

Regarding Claim 3, Walt et al teach the composition wherein the sites are separated by a distance of less than 15 m m (Fig. 5).

Regarding Claim 4, Walt et al teach the composition wherein said sites are separated by a distance of less than 15m m (Fig. 5) but they do not teach the separation is at least 5m m.

However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation distance of Walt et al using routine experimentation to thereby derive an optimal separation distance (e.g. at least 5m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claims 6 and 7, Walt et al teach the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 2.2m m (Fig. 5) which is less than 100m m as claimed in Claim 7 but they do not specifically teach the distance between centers is at least 5m m (Claim 6) and less than about 100m m (Claim 7). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Walt et al using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5m m and less than 100m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 8, Walt et al teach the composition wherein the substrate further comprises first and second assay locations (i.e. wells) and wherein said first and second subpopulations are distributed in said assay locations (page 22, lines 8-30).

Regarding Claim 9, Walt et al teach the composition wherein the distance between a first and second microsphere is less than 100 m m (Fig. 5).

Regarding Claim 10, Walt et al teach the composition wherein the distance between a first and second microsphere is less than 50 m m (Fig. 5).

Regarding Claim 11, Walt et al teach the composition wherein the distance between a first and second microsphere is less than 15 m m (Fig. 5).

Regarding Claim 12, Demers et al teach the composition wherein the distance between centers of a first and second subpopulations is at least 2.2m m (Fig. 5) but they do not specifically teach the distance between centers is at least 5m m. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Walt et al using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

Regarding Claim 18, Walt et al teach a method for making a composition comprising: providing a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μ (Fig. 5); and randomly distributing a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive (page 17, line 13-page 18, line 24). Walt et al teach that the substrate comprises a plurality of fibers arranged into a bundle for optimal observation via their microscope objective lens (page 19, lines 15-25) but they do not teach their substrate is formatted to the dimensions of a microscope slide. However, it was well known in the art at the time the claimed invention was made that fiber optic bundles can be formatted to desired dimensions as taught by Noonan et al. (Abstract) and Van Ness et al teach a motivation for formatting the substrate to have the dimensions of a microscope slide i.e. a substrate having the dimensions of a glass slide is easily illuminated and detected using a microscope (Column 19, lines 27-41). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply

the glass slide dimensioned substrate of Van Ness et al to the substrate of Walt et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 19, lines 27-30).

The courts have stated that claimed dimensions of a known device do not distinguish over the prior art device when the claimed device would not perform differently from the prior art device. *In Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

The courts have stated that absent evidence to the contrary, a particular configuration of a known device is a matter of choice which would have been obvious to one skilled in the art. *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966) (The court held that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.).

Regarding Claim 19 Walt et al teach the method wherein said wells are separated by distance of less than 25m m (Fig. 5).

Regarding Claim 20 Walt et al teach the method wherein said wells are separated by distance of less than 15m m (Fig. 5).

Regarding Claims 23 and 24, Walt et al teach the method wherein the distance between centers of a first and second subpopulations is at least 2.2m m (Fig. 5) but they do not specifically teach the distance between centers is at least 5m m (Claim 23) and at least 15 m m (Claim 24). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Walt et using routine experimentation to thereby derive an

optimal center-to-center distance (e.g. at least 5m m and at least 15m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 25, Walt et al teach the method wherein the distance between microspheres is at least 2.2m m (Fig. 5) but they do not specifically teach the distance between microspheres is at least 50m m. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between microspheres on the substrate of Walt using routine experimentation to thereby derive an optimal distance (e.g. at least 50m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

10. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 998/40726, published 17 September 1998) in view of Noonan et al (U.S. Patent No. 6,129,896, filed 17 December 1998) and Gentalen et al (U.S. Patent No. 6,306,643 B1, filed 24 August 1998).

Regarding Claims 21 and 22, Walt et al is silent regarding a ratio between microsphere subpopulations. However, ratios of subpopulations were well known in the art at the time the claimed invention was made as taught by Gentalen et al who teach that subpopulation ratios are derived based on experimental design (Column 11, lines 13-44 and Claim 9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was

made to modify the ratio of first and second subpopulations based on experimental design to thereby optimize experimental results. For example, for an experiment designed to detect nucleic acid sequences expressed in low copy number, the skilled practitioner in the art would have been motivated to provide subpopulations of nucleic acid microspheres in a ratio of 1:36 or 1:100 (high copy number sequence:low copy number sequence) to thereby detect the low copy number sequence without signal interference from the high copy number sequence. In this experimental design it would have been obvious to one of ordinary skill in the art to modify the low copy to high copy number ratio using routine experimentation to thereby optimize experimental conditions and to maximize detection of low copy number.

11. Claims 1-4, 6-12, 18-20 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chee et al (WO 00/39587, published 6 July 2000) in view of Demers et al (U.S. Patent No. 5,840,256, issued 24 November 1998) and Van Ness et al (U.S. Patent No. 6,248,521, issued 19 June 2001).

Regarding Claim 1, Chee et al teach a composition comprising: a substrate with a surface comprising discrete sites and a population of microspheres comprising at least a fist and a second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein the microspheres are randomly distributed on said substrate (Claim 1 and page 8, lines 13-27). Chee et al are silent regarding the substrate dimensions and therefore they do not specifically teach the substrate is formatted to the dimensions of a microscope slide. However, it was well known in the art a the time the claimed invention was made that microspheres on substrate having the dimensions of a glass slide are easily illuminated and detected using a microscope as taught by Van Ness et al (Column 19, lines 27-41). It would have been obvious to one of ordinary skill in

the art at the time the claimed invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Chee et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 19, lines 27-30). Chee et al are also silent regarding the distance between sites. However, Demers et al teach a similar composition comprising a substrate and a population of microspheres wherein the substrate comprises said site separated by a distance of less than 50m m (Column 4, lines 14-23 and Fig. 1) wherein the distance is optimized based on substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means (Column 4, line 59-Column 5, line 15). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the less than 50m m distance between sites on the substrate of Demers et al to the substrate of Chee et al thereby optimizing spacing based on substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means as taught by Demers et al (Column 4, line 59-Column 5, line 15) for the expected benefits of maximizing experimental results.

Regarding Claim 2, Demers et al teach the composition wherein said sites are separated by a distance of less than 25m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 3, Demers et al teach the composition wherein said sites are separated by a distance of less than 15m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 4, Demers et al teach the composition wherein said sites are separated by a distance of less than 15m m (Column 4, lines 14-23 and Fig. 1) but they do not teach the separation is at least 5m m. However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation distance of Demers using routine experimentation to thereby derive an optimal separation distance (e.g. at

least 5m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claims 6 and 7, Demers et al teach the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 2.2m m (Column 4, lines 20-21) which is less than 100m m as claimed in Claim 7. And they teach the pitch is determined/selected based on a number of factors e.g. substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means (Column 4, line 59-Column 5, line 15) but they do not specifically teach the distance between centers is at least 5m m (Claim 6) and less than about 100m m (Claim 7). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Demers using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5m m and less than 100m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 8, Demers et al teach the composition wherein said substrate further comprises first and second assay locations (i.e. cell) wherein said first and second subpopulations are distributed in said assay locations (Claim 1).

Regarding Claim 9, Demers et al teach the composition wherein the distance between the first and second microsphere is less than 100m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 10, Demers et al teach the composition wherein the distance between the first and second microsphere is less than 50m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 11, Demers et al teach the composition wherein the distance between the first and second microsphere is less than 15m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 12, Demers et al teach the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 2.2m m (Column 4, lines 20-21) and they teach the pitch is determined/selected based on a number of factors e.g. substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means (Column 4, line 59-Column 5, line 15) but they do not specifically teach the distance between centers is at least 5m m (Claim 6). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Demers using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

Regarding Claim 18, Chee et al teach a method for making a composition comprising: providing a substrate with a surface comprising discrete sites and randomly distributing a population of microspheres comprising at least a fist and a second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein the microspheres are randomly distributed on said substrate (Claim 1 and page 8, lines 13-27). Chee et al are silent regarding the substrate dimensions and therefore they do not specifically teach the substrate is formatted to the dimensions of a microscope slide. However, it was well known in the art a the time the claimed invention was made that microspheres on substrate having the dimensions of a glass slide are easily illuminated and detected using a microscope as taught by Van Ness et al (Column 19, lines 27-41). It would have been obvious to one of ordinary skill in the art at the time the claimed

invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Chee et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 19, lines 27-30). Chee et al are also silent regarding the distance between sites. However, Demers et al teach a similar composition comprising a substrate and a population of microspheres wherein the substrate comprises said site separated by a distance of less than 50m m (Column 4, lines 14-23 and Fig. 1) wherein the distance is optimized based on substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means (Column 4, line 59-Column 5, line 15). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the less than 50m m distance between sites on the substrate of Demers et al to the substrate of Chee et al thereby optimizing spacing based on substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means as taught by Demers et al (Column 4, line 59-Column 5, line 15) for the expected benefits of maximizing experimental results.

Regarding Claim 19, Demers et al teach the method wherein said wells are separated by a distance of less than 25m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claim 20, Demers et al teach the method wherein the wells are separated by a distance of less than 15m m (Column 4, lines 14-23 and Fig. 1).

Regarding Claims 23 and 24, Demers et al teach the method wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 2.2m m (Column 4, lines 20-21) and they teach the pitch is determined/selected based on a number of factors e.g. substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means (Column 4, line 59-Column 5, line 15) but they do not specifically teach the distance between centers is at least 5m m (Claim 23)

and at least 15 m m (Claim 24). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Demers using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5m m and at least 15m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller,* 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 25, Demers et al teach the method wherein the distance between microspheres is at least 2.2m m (Column 4, lines 20-21) and they teach the spacing is determined/selected based on a number of factors e.g. substrate size, surface area required the sites and site construction, surface area required for sealing/isolation and compatibility with illumination means (Column 4, line 59-Column 5, line 15) but they do not specifically teach the distance between microspheres is at least 50m m. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between microspheres on the substrate of Demers using routine experimentation to thereby derive an optimal distance (e.g. at least 50m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

12. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chee et al (WO 00/39587, published 6 July 2000) in view of Demers et al (U.S. Patent No. 5,840,256, issued 24 November 1998), Van Ness et al (U.S. Patent No. 6,248,521, issued 19 June 2001) and Gentalen et al (U.S. Patent No. 6,306,643 B1, filed 24 August 1998).

Regarding Claims 21 and 22, Chee et al is silent regarding a ratio between microsphere subpopulations. However, ratios of subpopulations were well known in the art at the time the claimed invention was made as taught by Gentalen et al who teach that subpopulation ratios are derived based on experimental design (Column 11, lines 13-44 and Claim 9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the ratio of first and second subpopulations based on experimental design to thereby optimize experimental results. For example, for an experiment designed to detect nucleic acid sequences expressed in low copy number, the skilled practitioner in the art would have been motivated to provide subpopulations of nucleic acid microspheres in a ratio of 1:36 or 1:100 (high copy number sequence:low copy number sequence) to thereby detect the low copy number sequence without signal interference from the high copy number sequence. In this experimental design it would have been obvious to one of ordinary skill in the art to modify the low copy to high copy number ratio using routine experimentation to thereby optimize experimental conditions to maximize detection of low copy number sequences.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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June 12, 2002

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